Also submitted herewith in full compliance to 37 C.F.R. §§1.821-1.825 is a disk copy of the substitute Sequence Listing. The disk copy of the substitute Sequence Listing, file "2921-0130P.ST25", is identical to the paper copy, except that it lacks formatting.

The substitute Sequence Listing includes the sequences disclosed in the figures as filed that were not made part of the original Sequence Listing. The amendments to the Specification are being made to reference the sequences by their SEQ ID NOS. These amendments are editorial in nature and do not constitute new matter.

Entry of the above amendments is earnestly solicited. An early and favorable first action on the merits is earnestly solicited.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Respectfully submitted,

BIRCH, STEWART, KOLASCH & BIRCH, LLP

By #32,668
Gerald M. Murphy, Jr.

P.O. Box 747
Falls Church, VA 22040-0747
(703) 205-8000

GMM/KW
2921-0130P

Attachments: Paper and disk copy and of Sequence Listing
Copy of Notice to Comply
Version with Markings to Show Changes Made

VERSION WITH MARKINGS TO SHOW CHANGES MADE

The paragraph beginning on page 5, line 22 has been amended as follows:

--Figure 2A discloses an amino acid sequence comparison of the human PTCH2 (residues 1-633 0f SEQ ID NO:1)(upper lines) and PTCH1(residues 1-699 of SEQ ID NO:6) (lower lines) sequences. --

The paragraph beginning on page 5, line 24 has been amended as folllows:

--Figure 2B is a representation of the alternative splicing events (SEQ ID NOS:7, 8, 9, 10, and 11) that result in different C-termini.--

The paragraph beginning on page 18, line 8 has been amended as follows:

--Detailed description of the drawings

Figure 1 shows the genomic sequence of SEQ ID NO:5, wherein exons and introns are designated in the genomic sequence of the present human patched 2 gene. However, exons 12a and 12b discussed above are not specifically shown in Figure 1, but is instead disclosed as the separate sequences SEQ ID NO:3 and SEQ ID NO:4, respectively. Figure 2A discloses an amino acid sequence comparison of the human PTCH2(residues 1-633 0f SEQ ID NO:1) (upper lines) and PTCH1(residues 1-699 of SEQ ID NO:6) (lower lines) sequences. Vertical lines indicate identical amino acids, while dots similar amino acids. The PTCH2 sequence presented is composed of the original cDNA clones and of the products of the 5' RACE analysis.--

The paragraph beginning on page 18, line 19, has been amended as follows:

--Figure 2B is a representation of the alternative splicing events (SEQ ID NOS:7, 8, 9, 10, 11, 12, 13, 14, 15 and 16) that result in different C-termini. In the parotid gland and the colon, the penultimate and the last exon are canonically joined together. In fetal brain however the penultimate exon with part of the 3' intron functions as the terminal exon. The intronic sequence is shown by small letters with the flanking exonic by capital letters. Above the nucleotide sequence, the deduced amino acid sequence is shown, and below is the corresponding sequence of the mouse Ptch2. The conserved intronic dinucleotides are shown by bold letters and the termination signals

are indicated by asterisks. Note the absence of conservation of the position of the termination codons between the mouse and human PTCH2 sequences. The putative polyadenylation signals are also shown in this diagram. The genomic organization was obtained by analyzing BAC clones encompassing the PTCH2 gene.--